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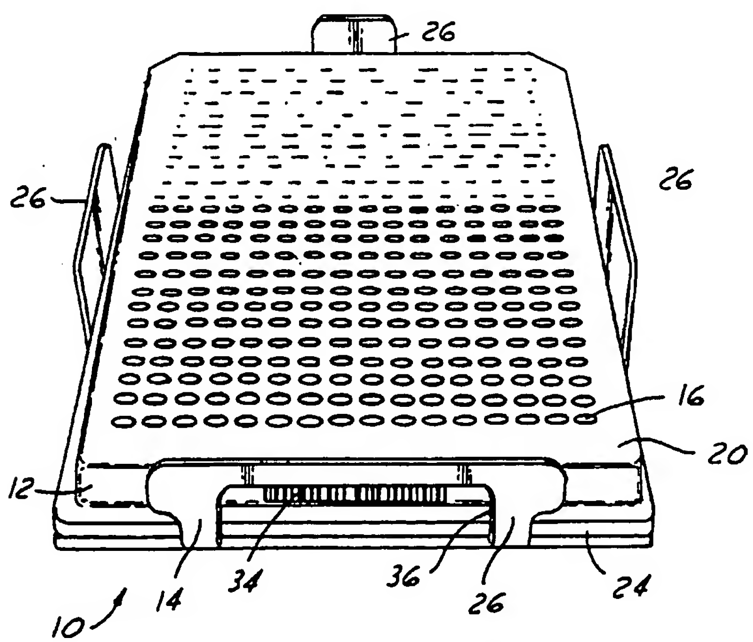
For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: WELL PLATE HOLDER



(57) Abstract: A well plate holder (10) has a generally planar bottom portion (24) having a first side, a second side, a third side and a fourth side. The first side has a first side wall portion (26) extending therefrom and the second side having a second side wall portion (26) extending therefrom. The third side may have a third side wall and the fourth side has a fourth side wall portion (26) extending therefrom. The first side wall may comprise dowel pins (28) and the second side wall may comprise a holding pin (30).

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WELL PLATE HOLDER

Technical Field

The present invention relates generally to a device holder used to manipulate a device during automated processing of the device, and more particularly, to a well plate holder particularly suited for robotic manipulation during processing.

Background Of The Invention

Methods of making a homologous series of compounds, or the testing of new potential drug compounds comprising a series of light compounds, has been a slow process because each member of a series or each potential drug must be made individually and tested individually. For example, a plurality of potential drug compounds that differ perhaps only by a single amino acid or nucleotide base, or a different sequence of amino acids or nucleotides are tested by an agent to determine their potential for being suitable drug candidates. These steps are typically performed manually which is both expensive and time consuming.

These processes require various stages of processing such as reagent mixing and thermal cycling. These processes may be carried out using a microtiter plate in which a number of wells may be used to carry out simultaneous processing. One size microtiter plate has 384 reagent wells in an area about 5 inches x 3.3 inches. Of course, various

numbers of wells may be contained in microtiter plates. For example, 1536 wells on a similar size plate may be used. Microtiter plates are most commonly formed of plastic material so they are lightweight and inexpensive. Methods for automating these processes include automated reagent loading, testing and manipulating such as thermal cycling.

Commonly known polymerase chain reaction (PCR) processes use a number of thermal cycles followed by cool down periods. Because the microtiter plates are made from plastic, the microtiter plates are subject to warpage. Warpage makes the plate difficult to manipulate, difficult to aspirate the fluid therein and difficult to dispense the fluid therefrom.

Because the microtiter plates are commonly formed of plastic material and have a low profile with an irregular cross section, a robotic manipulator may not easily or reliably grip the microtiter plate.

It would therefore be desirable to allow the well plate to be easily manipulated and to compensate any distortion of the well plate caused by thermocycling.

Summary Of The Invention

It is therefore one object of the invention to provide improved robotic manipulation of a well plate.

In one aspect of the invention, a well plate holder has a generally planar bottom portion having a first side, a second side, a third side and a fourth side. The first side has a first side wall extending therefrom and the second side has a second side wall extending therefrom. The third and fourth sides also have a respective side wall. The side walls are sized so that a robotic manipulator may easily grasp them to hold and manipulate the holder and the well plate therein.

One feature of the invention is that said first side wall may comprise dowel pins and the second side wall may comprise a holding pin.

In a further aspect of the invention, an analysis system has a robot having a robotic manipulator. A plate holder is sized to receive a well plate and has a generally planar bottom portion. The bottom portion has four sides with respective side walls extending therefrom. The first and second side walls have respective dowel pins and holding pins for retaining the plate to the plate holder. Each side wall is sized to be gripped by the fingers of the robotic manipulator.

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Fig. 6 is a perspective view of a first embodiment of a well plate holder.

Fig. 7 is a side view of a dowel pin.

Fig. 8 is a side view of a second pin.

Fig. 9 is a perspective view of a second embodiment of a well plate holder.

Fig. 10 is a top view of a well plate holder according to a third embodiment of the invention.

Fig. 11 is an elevational view of an end bar of Fig. 10.

Fig. 12 is a perspective view of a fourth embodiment of a well plate according to the present invention.

Fig. 13 is a fifth embodiment of a well plate holder according to the present invention.

Detailed Description of the Preferred Embodiment

In the following figures, the same reference numerals will be used to identify identical components. The present invention is described with respect to a well plate. The well plate is defined as a microtiter plate, PCR plate or other plates having a plurality of wells therein. The plate may also comprise a multilayer microfluidic plate.

Referring now to Fig. 1, a well plate/well plate holder assembly 10 is illustrated having a well plate 12 and a well plate holder 14. Well plate holder 14 is sized to receive and hold well plate 12 therein. Well plate 12 has a plurality of wells 16 arranged in rows and columns. As shown, 384 wells are arranged in 16 rows and 24 columns. Of course, the number of wells may vary depending on the process to be carried out. The filling of wells 16 may be automated as part of the process. Well plate 12 is preferably formed of a plastic material. The plastic material is preferred due to its light weight. However, the plastic material has a tendency to become distorted or warped during thermal cycling. The present invention is used to reduce warpage in the plate.

Well plate 12 has a ridge 18 that extends around the perimeter. Ridge 18 does not extend the same distance from well plate holder 14 as does a top surface 20. That is, the ridge 18 has a thickness less than well plate. Well plate 12 has a plurality of receiving holes 22 formed therein. Commonly, receiving holes 22 are located two on each edge.

Well plate holder 14 has a generally planar bottom portion or base 24 with a plurality of side walls 26 extending therefrom. Preferably, side walls 26 extend in a perpendicular direction from the plane of base 24. The side walls extend a distance above base 24 a distance to allow manual gripping as well as by a robotic manipulator as will be further

described below. At least one side wall 26 has dowel pins 28 that extend into receiving holes 22. One sidewall 26 has holding pins 30. Holding pins 30 are used to hold ridge 18 and therefore the well plate 12 to base 24 of well plate holder 14. If a ridge 18 is not present on well plate 12, holding pins 30 may be positioned to hold top surface 20 against base 24.

Referring now to Fig. 2, well plate 12 has a bar code 34 positioned on one side thereof. Bar code 34 is used by the automated equipment to identify the particular well plate 12 and the reagent therein. One sidewall 26 preferably has a bar code opening 36 to allow a bar code reader in the automated equipment to read bar code 34. Bar code 34 is preferably located on a lateral side of well plate 12.

Referring now to Fig. 3, a perspective view of an automated processing system 40 is illustrated. Automated processing system has a robot 42 with an arm 44 and a robotic manipulator 46. Robotic manipulator 46 has gripping fingers 48 that extend therefrom and are used to grip side wall 26 of well plate holder 14. Fingers 48 grip the side walls 26 of well plate holder 14 to manipulate well plate/well plate holder assembly 10. The side walls 26 are sized so that well plate holder 14 is securely held during manipulation. For example, robot 42 may be used to position assembly 10 within a rack 50 or in a bar code reader 52. Rack 50 may be a multilevel thermal cycling rack.

Referring now to Fig. 4, as illustrated, fingers 48 are gripping lateral side walls 26 so that bar code 34 is still visible within bar code opening 36.

Referring now to Fig. 5, robotic manipulator 46 is illustrated with fingers 48 gripping longitudinal walls 26. Gripping either longitudinal walls or lateral walls may be desirable at various stages of processing.

Referring now to Fig. 6, a first embodiment 60 of a well plate holder 14 is illustrated. Well plate holder 14 is preferably formed of a light weight and rigid material such as aluminum. In one constructed embodiment, 2024 aluminum having a 0.08 inch thickness was used to construct well plate holder 14. Both side wall and base 24 are preferably constructed from the same material although different materials may be used. In this embodiment, side wall 26 are integrally formed with based 24. The first lateral sidewall 26 has bar code opening 36 and dowel holes 62. The first lateral side wall 26 may be mushroom-shaped. That is, dowel holes 62 may be mounted on laterally extending radially shape portions 61 that extend from a base portion 63. The width of portion 61 is thus greater than the width of base portion 63.

A second lateral sidewall 64 is positioned opposite lateral sidewall 26. Lateral sidewall 64 in

this embodiment is comprised of three disparate portions; a pair of holding walls 66 and a center wall 68. Center wall 68 is positioned between the holding pin walls 66. Preferably, holding pin walls 66 and center wall 68 are separated by a space. A robotic manipulator may be used to grip holding walls 66 and center wall 68. A pair of finger slots 70 are formed in base 24 between respective holding pin wall 66 and center wall 68. Finger slots 70 increase the manual maneuverability of well plate holder 14.

Base 24 preferably has a plurality of cutouts 72. As illustrated, six cutouts are formed in base 24. Cutouts 72 are illustrated as oval shaped. However, various shapes and numbers of cutouts 72 may be formed. Cutouts 72 are used to reduce the weight of the well plate. The existence, the size and shape of the cutouts may vary as would be evident to those skilled in the art.

Holding pin wall 66 has holding pin hole 74 positioned therein. Holding pins 30 are preferably press fit into holding pin hole 74. Of course, holding pins may be coupled to side wall 26 in a variety of ways including securing with a fastener or adhesive or integrally forming them therewith.

Referring now to Fig. 7, a dowel pin 28 that is to be received within dowel holes 62 of Fig. 6 is illustrated. Dowel pin 28 has an end portion 76 sized to be received within dowel hole 62. Dowel pin 28 has a body portion 78 having an insertion end 80

that is tapered to assist in the insertion of dowel pin 28 within receiving holes 22 of well plate. In the constructed embodiment, dowel pins 28 were formed of stainless steel.

Referring now to Fig. 8, a holding pin 30 is illustrated. Holding pin 30 has a diameter to be received within holding pin hole 74 as shown in Fig. 6. Holding pin 30 has a body 82 with an axially extending wall 84 and a rounded end 86. Axially extending wall 84 is used to position ridge 18 of well plate 12 between it and base 24. Rounded end 86 is provided to reduce the sharp edge and prevent damage to well plate 12. In the constructed embodiment, holding pins 30 were formed of stainless steel.

Referring now to Fig. 9, a second embodiment 60' of a well plate holder is illustrated. The well plate holder is similar in every aspect with that illustrated in Fig. 6 except that one cutout 72' is provided rather than a plurality of cutouts. Cutout 72' has a rectangular shape. In this manner, well plate holder 14' has a reduced weight from that shown in Fig. 6.

Referring now to Figs. 10 and 11, a third embodiment 60 is shown. The third embodiment 60 is similar in every respect to that illustrated in Fig. 6, including lateral wall 64 and longitudinal side wall 26. However, one lateral wall 26 is illustrated as a separate component. Sidewall 26

preferably has a similar shape as that shown in Fig. 6 except that two fastener holes 88 are provided therethrough. Fastener holes 88 align with fastener channels 90 formed in base 24. Fastener holes 88 and fastener channels 90 each receive a fastener 92 to secure lateral wall 26 to base 24.

Referring now to Fig. 12, a fourth embodiment 60''' is illustrated. Fourth embodiment 60''' has a well plate holder 14 similar to that shown in Fig. 6 above except lateral walls are formed differently. In lateral wall 94, a bar code opening 36 has not been provided. Lateral wall 96 is formed of a single wall positioned between finger slots 70''. Lateral wall 96 has holding pin holes 74 positioned therein similar to that shown above.

Referring now to Fig. 13, a fifth embodiment 60'''' is illustrated. Fifth embodiment 60''' is similar to that illustrated in Fig. 9 in that a single cutout opening 72' positioned within based 24. In this embodiment, however, lateral walls 98 are formed of a pair of extensions 100. Extensions 100 do not have a holding pin hole 74 or dowel hole 62 as shown above. In this manner, no downward force is provided to hold a well plate within well plate holder 14. The fifth embodiment is suitable for use prior to thermal cycling performed on the well plates.

In operation, well plates 12 are typically provided preloaded with reagents. A microseal film

is formed across the top surface 20 of well plate 12. Well plates 12 are manually inserted into well plate holder 14. Preferably, the liquids within the wells do not contact the film seal during insertion. Preferably, the well plate 12 is positioned within well plate holder 14 at about a 20 degree angle so that the dowel pins 28 align with receiving holes 22. The well plate 12 and well plate holder 14 may be placed in a centrifuge to spin down the liquids in the wells. The finger slots 70 may be used to grip the well plate holder 14 while the well plate 12 is pushed under holding pins 30. Preferably, each holding pin 30 is positioned on well plate in turn. Holding pins 30 and dowel pins 28 mitigate the effects of warping during thermal cycling as well as said well plate 12 during manipulation. That is, the well plate holder can hold the well plate in straightened position if warping has occurred. Well plate holder may also prevent warping from occurring. Both pairs of side wall 26 allow the well plate holder 14 to be gripped during robotic manipulation.

The well plate 12 and well plate holder 14 may be used together with a variety of processing devices such as a bar code reader/regrip station, a carousel or multimeter.

While particular embodiments of the invention have been shown and described, numerous variations and alternate embodiments will occur to those skilled in the art. Accordingly, it is intended that the invention be limited only in terms of the appended claims.

What Is Claimed is:

1. A holder for holding a well plate comprising:

a generally planar bottom portion;

said bottom portion having a first side, a second side, a third side and a fourth side;

said first side having a first side wall portion extending therefrom; and

said second side positioned opposite said first side wall, said second side having a second wall portion extending therefrom;

said third side having a third side wall; and

said fourth side having a fourth side wall position opposite said third side wall.

2. A holder as recited in claim 1 wherein said first side wall, said second side wall, said third side wall and said fourth side wall are integrally formed with said base plate.

3. A holder as recited in claim 1 wherein said first side wall is a separately attached component.

4. A holder as recited in claim 1 wherein said first side wall comprises dowel pins.

5. A holder as recited in claim 1 wherein said second side wall comprises a holding pin.

6. A holder as recited in claim 1 wherein said bottom portion comprises a finger slot.

7. A holder as recited in claim 1 wherein said second side wall comprises a center wall positioned between a pair of holding pin walls.

8. A holder as recited in claim 7 wherein said bottom portion comprises a pair of finger slots, one finger slot between one of said pair of holding pin wall and said center and the other one of said pair of holding pins walls and said center wall.

9. A holder as recited in claim 1 wherein said first side wall has a bar code opening therethrough.

10. A holder as recited in claim 1 wherein said bottom portion has a cutout therethrough.

11. A holder as recited in claim 1 wherein said bottom portion has a plurality of cutouts therethrough.

12. A holder as recited in claim 1 wherein said first side wall and said second side wall comprise a pair of extensions.

13. A plate holder comprising:

a generally planar bottom portion;

said bottom portion having a first side, a second side, a third side and a fourth side, said first side having a first side wall having dowel pins

extending therefrom and said second side wall positioned opposite said first side wall having holding pins extending therefrom, said third side having a third side wall and said fourth side having a fourth side wall extending therefrom.

14. A holder as recited in claim 13 wherein said bottom portion comprises a finger slot.

15. A holder as recited in claim 13 wherein said second side wall comprises a center wall positioned between a pair of holding pin walls.

16. A holder as recited in claim 15 wherein said bottom portion comprises a pair of finger slots, one finger slot between one of said pair of holding pin wall and said center and the other one of said pair of holding pins walls and said center wall.

17. A holder as recited in claim 13 wherein said first side wall has a bar code opening therethrough.

18. A well plate holder for use with a robotic manipulator having fingers, said well plate holder comprising:

a generally planar bottom portion;

said bottom portion having a first side, a second side, a third side and a fourth side, said first side having a first side wall having dowel pins extending therefrom and said second side wall positioned opposite said first side wall having

holding pins extending therefrom., said third side having a third side wall and said fourth side having a fourth side wall, said first sidewall, said second side wall, said third side wall and said fourth side wall sized to be gripped by said robotic manipulator.

19. A holder as recited in claim 18 wherein said bottom portion comprises a finger slot.

20. A holder as recited in claim 18 wherein said second side wall comprises a center wall positioned between a pair of holding pin walls.

21. A holder as recited in claim 20 wherein said bottom portion comprises a pair of finger slots, one finger slot between one of said pair of holding pin wall and said center and the other one of said pair of holding pins walls and said center wall.

22. A holder as recited in claim 8 wherein said first side has a bar code opening therethrough.

23. A analysis system comprising:

a robot having a robotic manipulator with movable fingers;

a plate;

a plate holder sized to receive said plate, said plate holder a generally planar bottom portion;

said bottom portion having a first side, a second side, a third side and a fourth side, said first side having dowel pins extending therefrom and said third side opposite said first side having

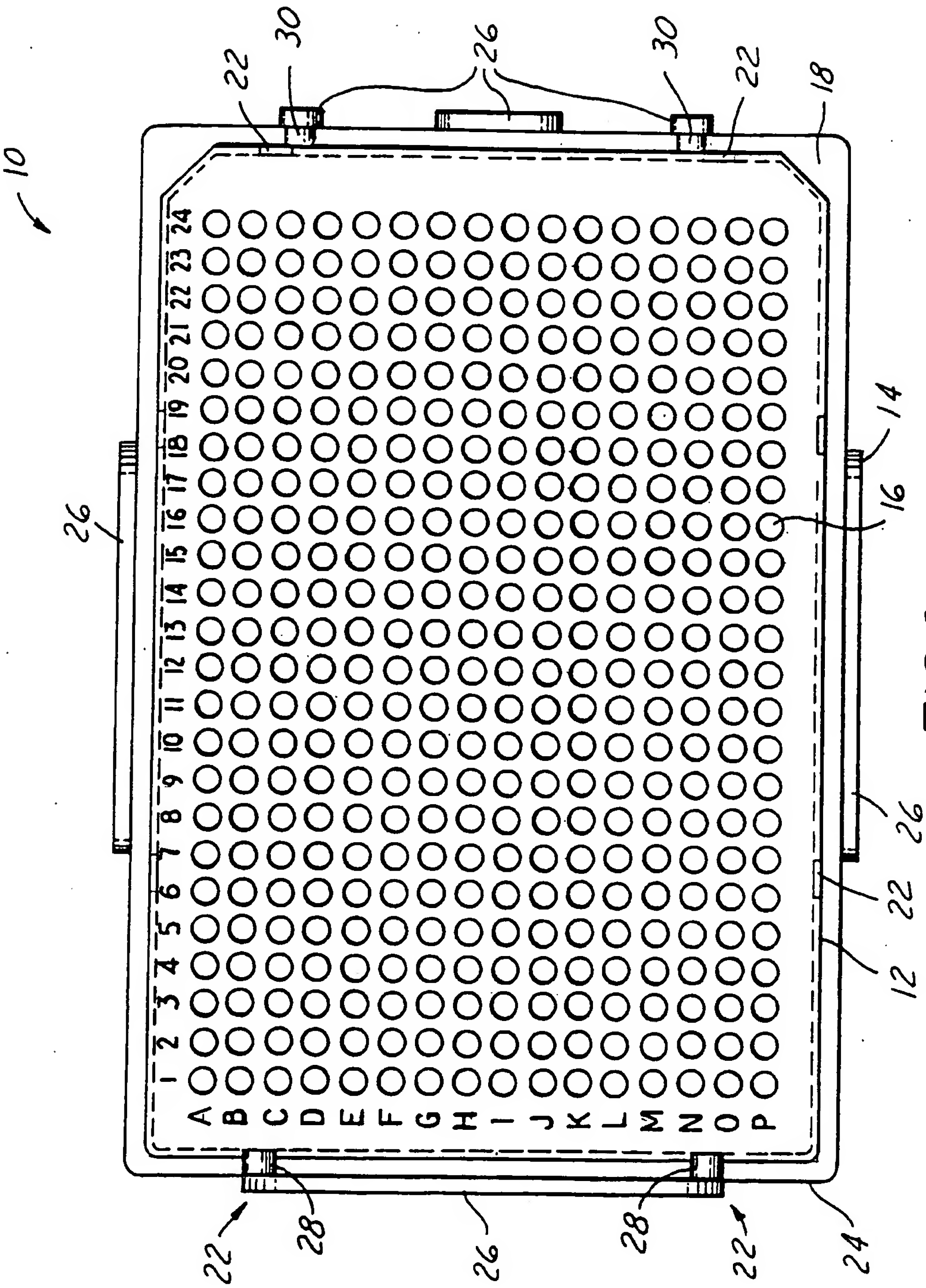
holding pins extending therefrom, said first side, said second side said third side and said fourth sized to be gripped by said fingers.

24. An analysis system as recited in claim 23 wherein said bottom portion comprises a finger slot.

25. An analysis system as recited in claim 23 wherein said second side wall comprises a center wall positioned between a pair of holding pin walls.

26. An analysis system as recited in claim 25 wherein said bottom portion comprises a pair of finger slots, one finger slot between one of said pair of holding pin wall and said center and the other one of said pair of holding pins walls and said center wall.

27. An analysis system holder as recited in claim 23 wherein said first side has a bar code opening therethrough.


10
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A B C D E F G H I J K L M N O P
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24

FIG.1

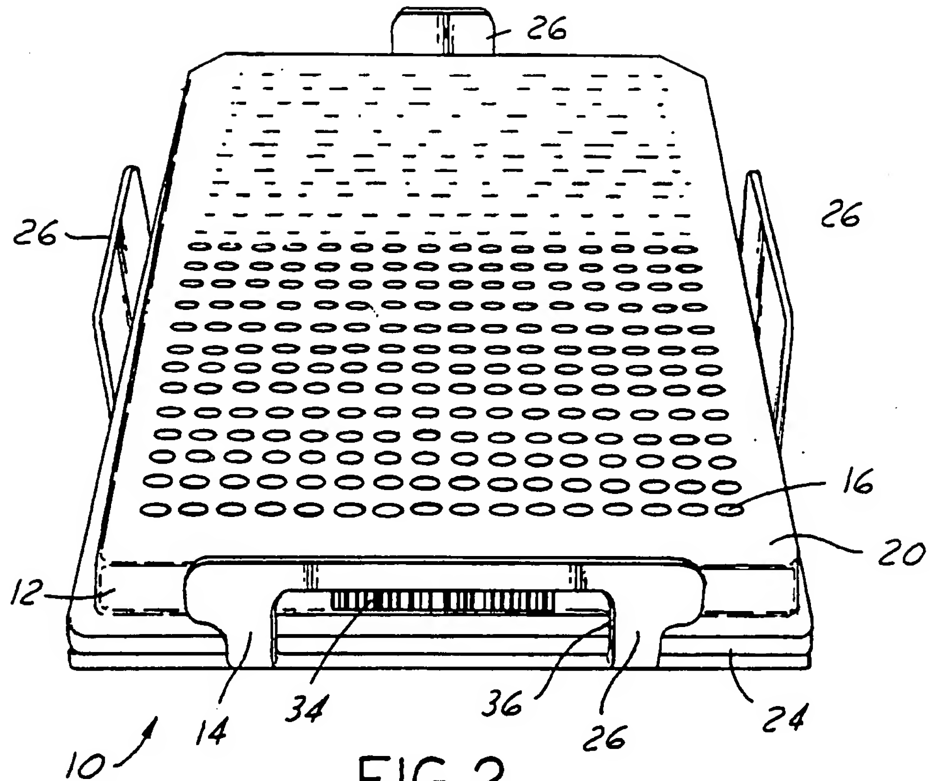

FIG.2

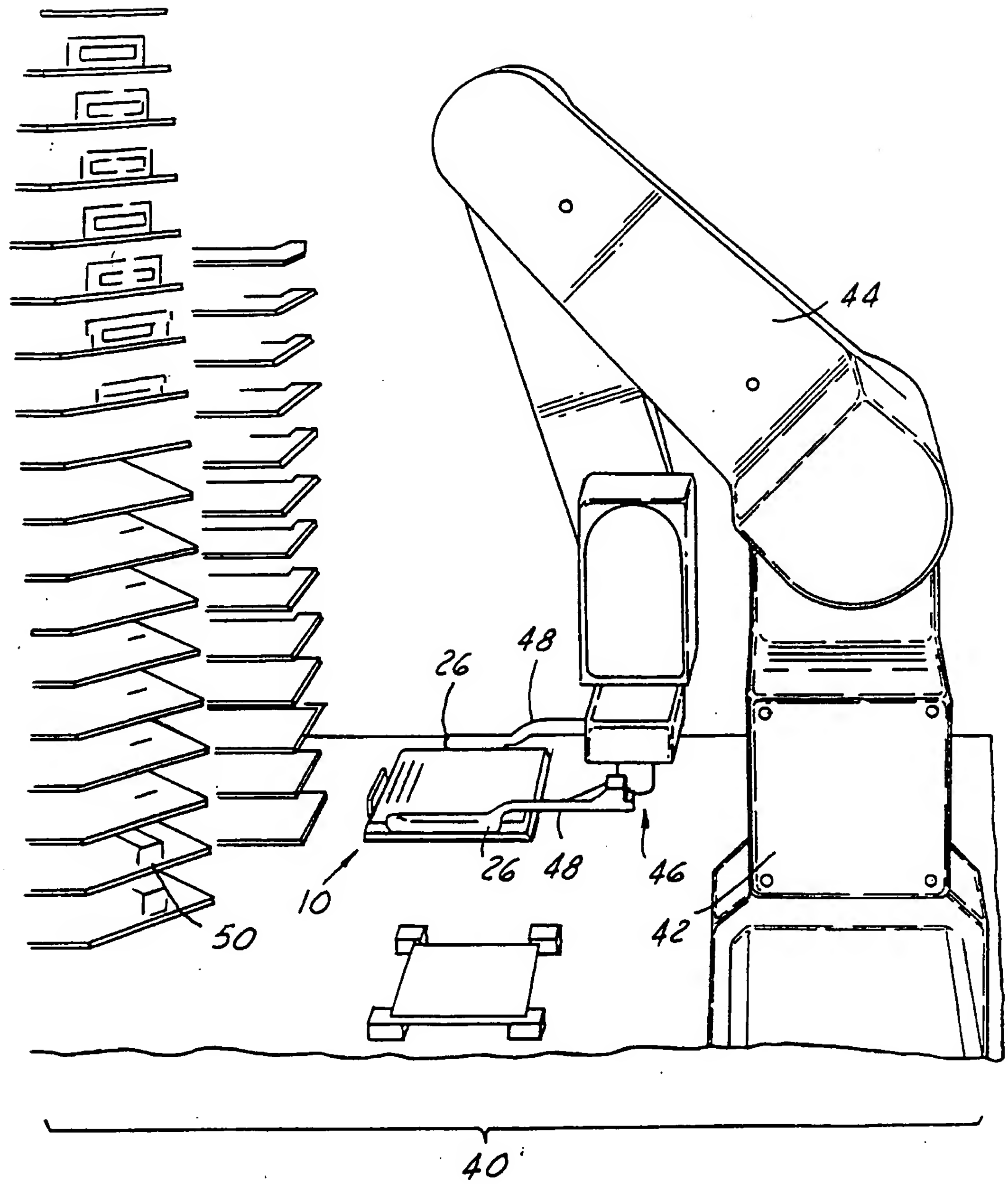

FIG.3

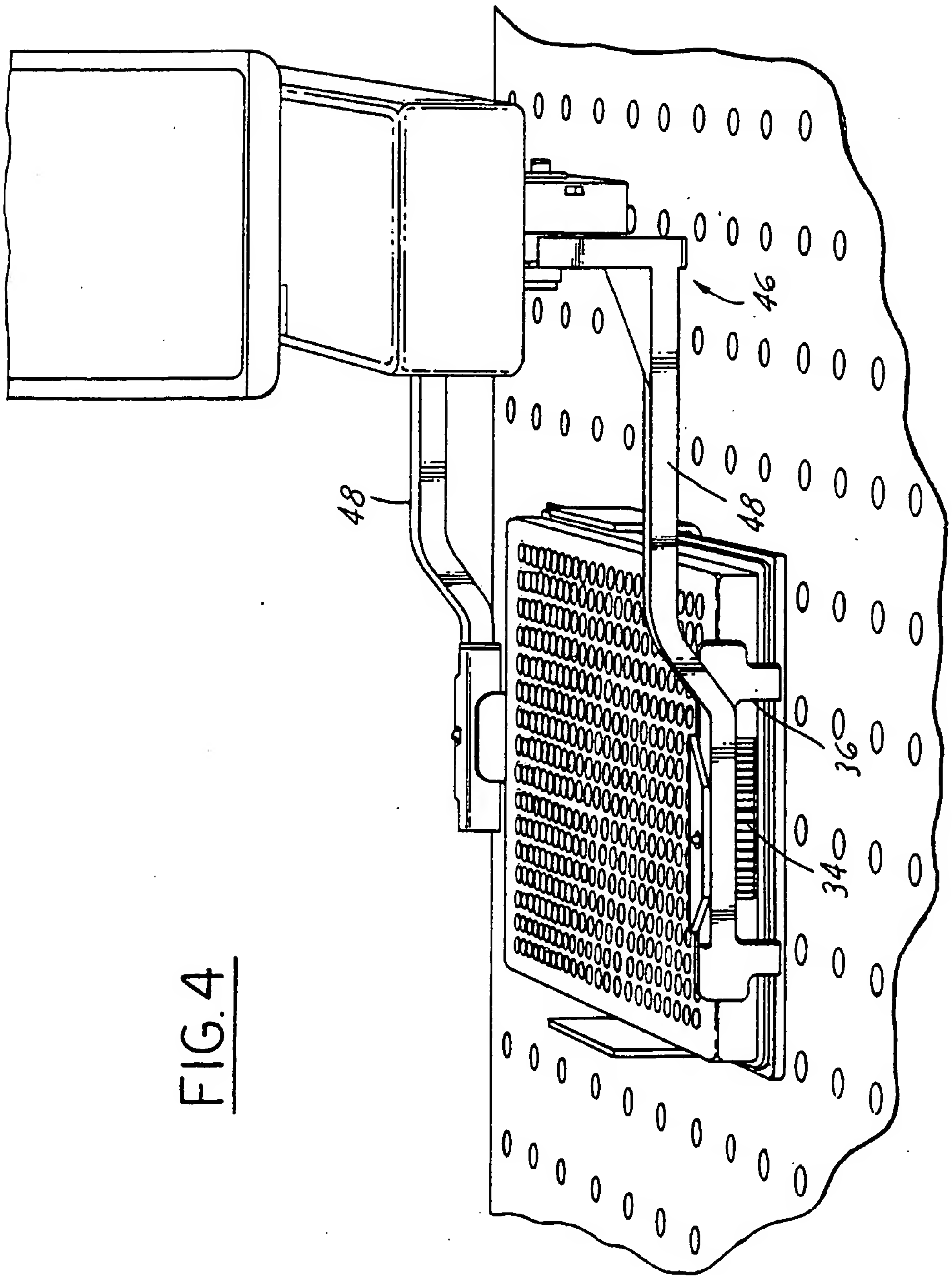

FIG. 4

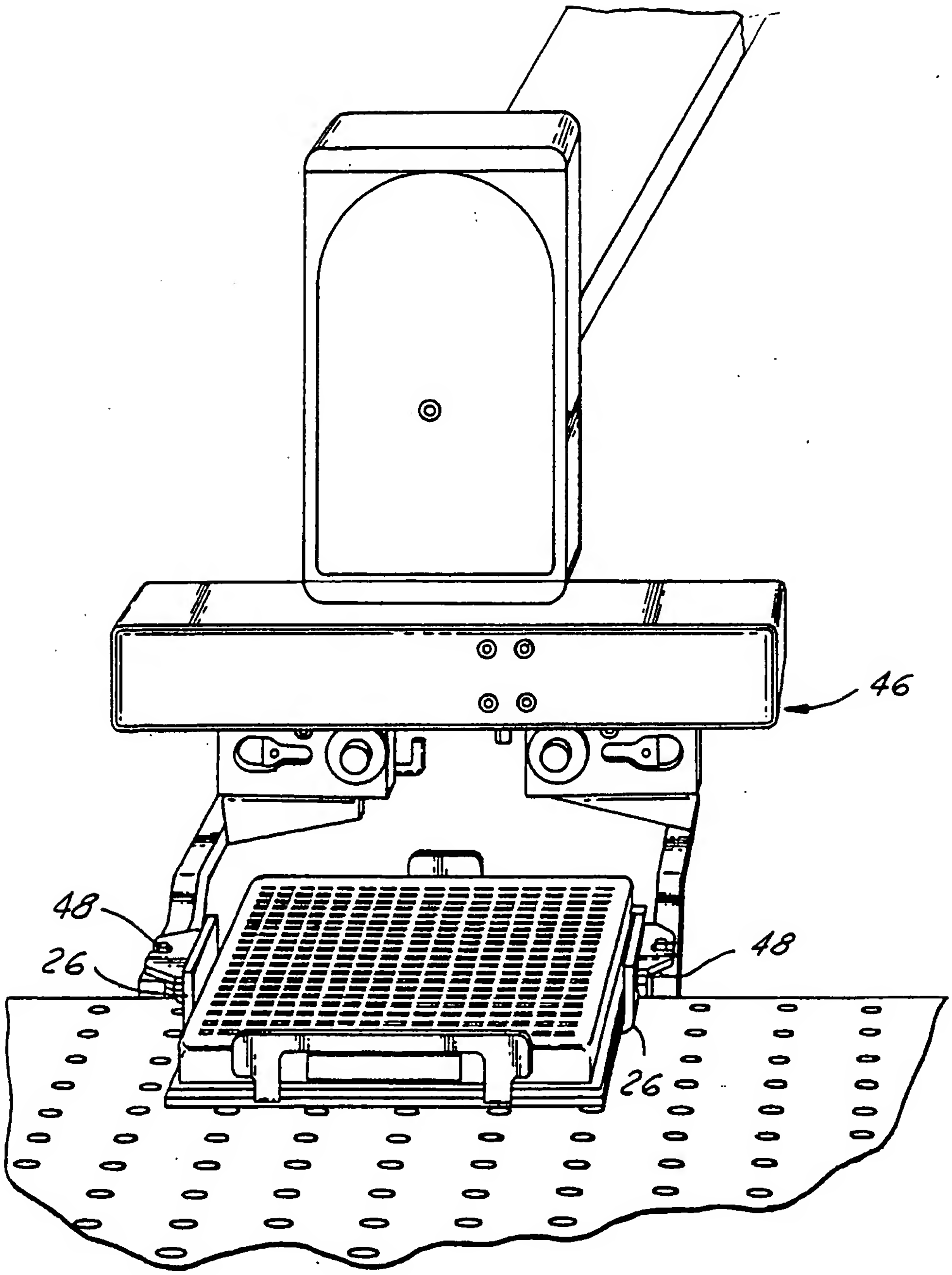

FIG.5

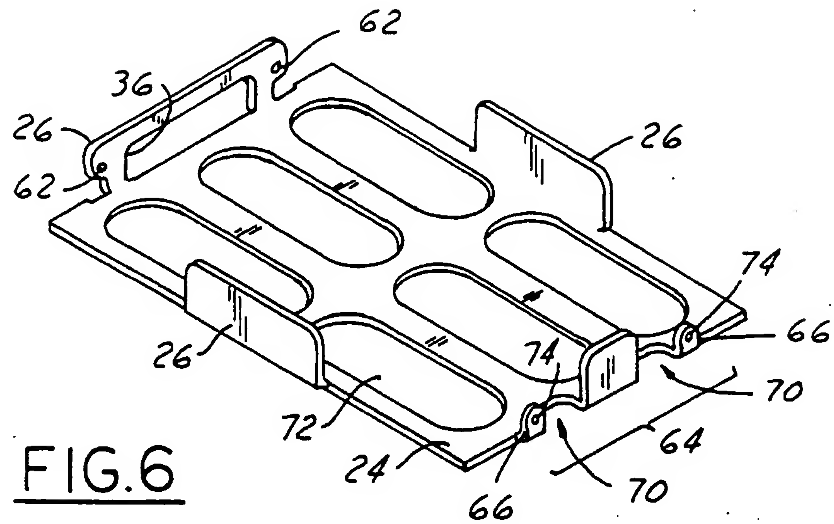

FIG.6

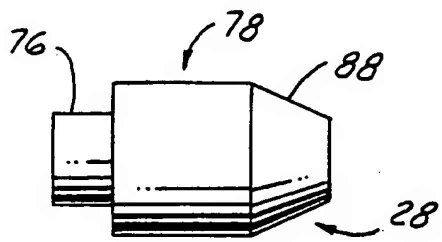

FIG.7

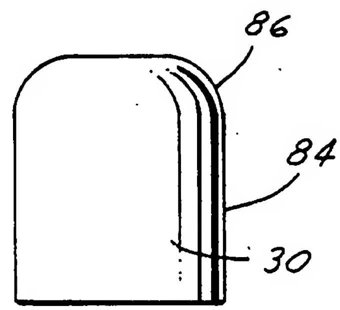

FIG.8

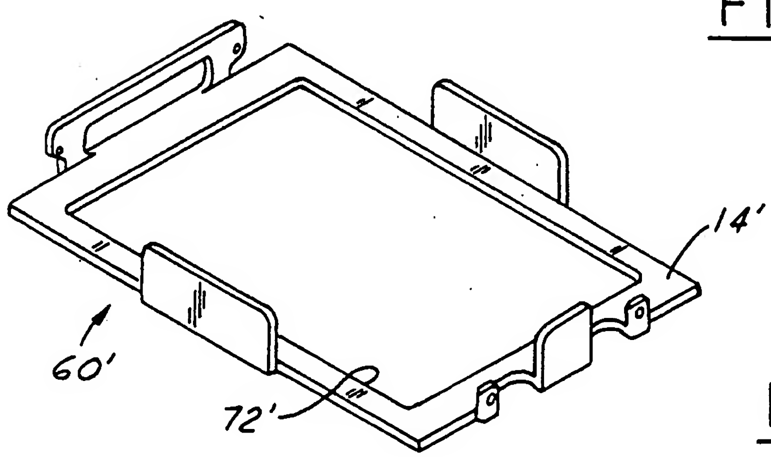

FIG.9

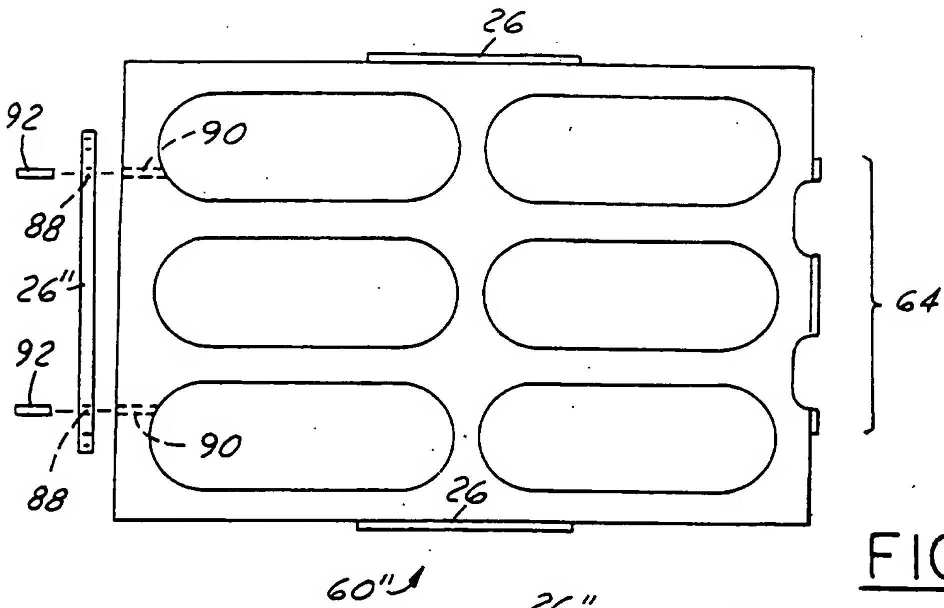

FIG.10

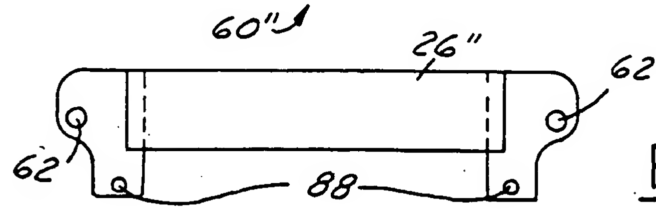

FIG.11

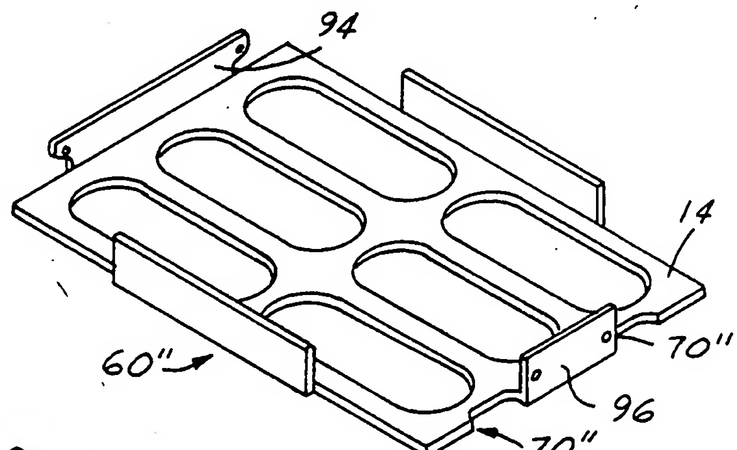

FIG.12

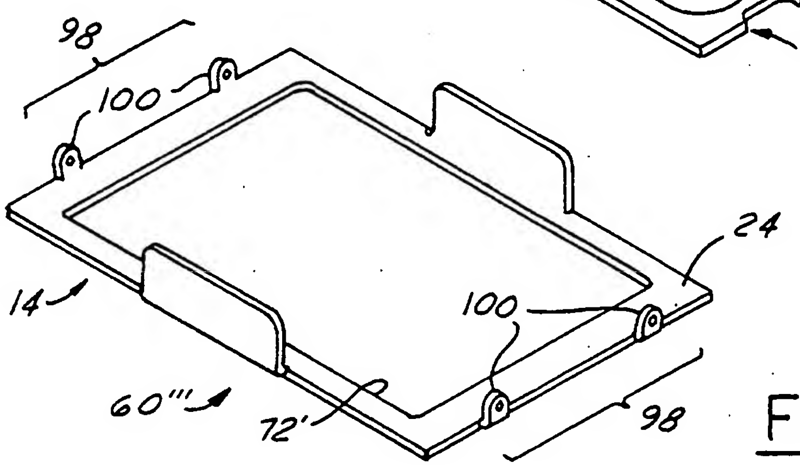

FIG.13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/40110

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :B01L 9/00
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 422/63, 64, 65, 102, 104; 435/288.4, 303.1, 305.1; 436/43, 47, 48, 809

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X.P	US 6,193,642 B1 (HRISTAKE) 27 February 2001, entire document.	1, 3-5, 9, 12-13, 17-18
X.P ----- Y,P	US 6,045,760 A (AIZAWA et al) 04 April 2000, entire document.	1-2 ----- 3-27
Y	US 5,961,926 A (KOLB et al) 05 October 1999, entire document.	6, 10-11, 14, 19, 24
Y,P	US 6,099,230 A (HITCH) 08 August 2000, entire document.	18-27
Y,P	US 6,121,054 A (LEBL) 19 September 2000, entire document.	1-27
Y	US 5,592,289 A (NORRIS) 07 January 1997, entire document.	1-27

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance		
"E"	earlier document published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
07 MAY 2001	08 JUN 2001

Name and mailing address of the ISA/US	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/40110

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

422/63, 64, 65, 102, 104; 435/288.4, 303.1, 305.1; 436/43, 47, 48, 809